Applicants assert that the specification provides sufficient support for the presently claimed invention. The Examiner has noted for the record that the specification is enabling for polynucleotides encoding HNF-6, OC-2, and OC-3. Applicants note that page 6, lines 24-32, describes the methods by which polynucleotides of the presently claimed invention may be administered to a patient or to cell lines of a patient via *ex vivo* treatment. The specification, page 7, lines 3-13, discloses methods for using the presently claimed pharmaceutical composition in cell therapy, *in vivo* and *ex vivo*. The specification further describes the components of the pharmaceutical composition on page 7, lines 14-34.

The specification has enabled the therapeutic component of the presently claimed pharmaceutical composition, and the specification discloses several pharmaceutical vehicles and methods of administration. Applicants assert that one of skill in the art would recognize that the method of administration, frequency of administration, the patient's physiological tolerance for the composition, and other factors dictate the components of a therapeutically effective pharmaceutical composition. Thus one of skill in the art would be capable of making and using the presently claimed invention by suiting the presently claimed invention to their specific application conditions.

The Examiner states that those of skill in this subject area are considered to be highly skilled, therefore Applicants assert that one of skill could use the specification of the present application along with their knowledge of pharmaceutical compositions and applications to make and use the presently claimed invention without undue experimentation. Applicants assert that the presently claimed invention is enabled and therefore respectfully request withdrawal of the rejection under 35 U.S.C. § 112, first paragraph.

Claim Rejection Under 35 U.S.C. § 102(b)

Claims 1 and 2 were rejected under 35 U.S.C. § 102(b) as being anticipated by Lemaigre et al. Lemaigre et al. disclose the nucleotide sequence of HNF-6. Claim 1 has been amended and no longer recites a pharmaceutical composition comprising the nucleotide sequence of HNF-6. Claim 1 as amended recites a pharmaceutical composition comprising an element selected from the group consisting of: a polynucleotide encoding OC-2, a vector comprising said polynucleotide, OC-2 having the amino acid sequence of SEQ ID NO:2, and a cell line transformed with said vector. Lemaigre et al. do not disclose SEQ ID NO:2 or OC-2. Claim 2

has been cancelled, thus the rejection is moot is regard to this claim. Applicants respectfully request withdrawal of the claim rejections on this basis.

Claim 2 was also rejected under 35 U.S.C. § 102(b) as being anticipated by Lannoy et al. Claim 2 has been cancelled, thus the rejection is moot.

Claims 3, 4, and 5 were rejected under 35 U.S.C. § 102(b) as being anticipated by Jacquemin et al. Applicants wish to note that anticipation under 35 U.S.C. § 102(b) requires that the claimed invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country more than one year prior to the date of application for patent in the United States. Applicants filed an International Application, designating the United States, on August 17, 1999 and entered the National Phase on February 20, 2001. The Jacquemin et al. reference was received for publication by the Journal of Biochemistry on October 21, 1998 and was published in January 1999. Thus, date of publication of the Jacquemin et al. reference is not more than one year prior to the date of application for patent in the United States, August 17, 1999. Applicants assert that the rejection of Claims 3, 4, and 5 is not proper under 35 U.S.C. § 102(b), thus Applicants respectfully request withdrawal of the rejection on this basis. Furthermore, the present application claims priority to an application filed in a WTO country prior to the publication date of the Jacquemin et al. reference. Thus, the invention date under 35 U.S.C. § 102(a) is necessarily prior to the publication of the Jacquemin reference. Specifically, the present application claims priority to Belgian application #9800609, filed August 17, 1998. Therefore, Applicants assert that the presently claimed invention is not anticipated under 35 U.S.C. § 102(a) nor 35 U.S.C. § 102(b) by the Jacquemin et al. reference.

Claim 6 was rejected under 35 U.S.C. § 102(b) as being anticipated by Krolewski. Krolewski discloses the use of plasmid and viral vectors carrying a polynucleotide of the ONECUT family, along with the use of cationic liposomes. However, Claim 6 is dependent on amended Claim 1 which recites a pharmaceutical composition comprising an element selected from the group consisting of: a polynucleotide encoding OC-2, a vector comprising said polynucleotide, OC-2 having the amino acid sequence of SEQ ID NO:2, and a cell line transformed with said vector. Krolewski does not disclose OC-2 or SEQ ID NO:2. Thus,

Applicants assert that the presently claimed invention is not anticipated by Krolewski. Applicants respectfully request withdrawal of the rejection on this basis.

Conclusion

In light of the forgoing remarks and amendments, Applicants assert that the present application in is condition for allowance. Should any issues arise which may delay prosecution of the present application, the Examiner is respectfully invited to contact the under-signed attorney at the telephone number below.

Please charge any additional fees, including any fees for additional extension of time, or credit overpayment to Deposit Account No. 11-1410.

Respectfully submitted,

KNOBBE, MARTENS, OLSON & BEAR, LLP

Dated: 5/3/02

By: _____

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VERSION WITH MARKINGS TO SHOW CHANGES MADE

Deletions are in **[bold and brackets]**, and insertions are underlined.

IN THE ABSTRACT:

Please insert the Abstract attached hereto, following the VERSION WITH MARKINGS TO SHOW CHANGES MADE, as page 19 of the application as filed.

IN THE CLAIMS:

Please cancel Claims 2 and 3.

Please amend the claims as follows:

1. **(AMENDED TWICE)** A pharmaceutical composition comprising an element selected from the group consisting of: a polynucleotide encoding **[a peptide of the ONECUT family]**OC-2, a vector comprising said polynucleotide, **[the polypeptide encoded by said polynucleotide]**OC-2 having the amino acid sequence of SEQ ID NO:2, and a cell line transformed with said vector.

4. **(AMENDED TWICE)** **[The]**A pharmaceutical composition **[of claim 1]**comprising an element selected from the group consisting of: a polynucleotide encoding OC-3, a vector comprising said polynucleotide, OC-3 having the amino acid sequence of SEQ ID NO: 3, and a cell line transformed with said vector **[wherein the protein of the ONECUT family is OC-3, the amino acid sequence of which is SEQ ID No. 3]**.

7. **(AMENDED TWICE)** A method for the prevention and/or for the treatment of type 1 or type 2 diabetes or of disorders linked to diabetes, for the prevention and/or for the treatment of cancer and for the prevention and for the treatment of Waardenburg syndrome, comprising:

administration of **[the]**a pharmaceutical composition **[of Claim 1]** in an amount effective to prevent or reduce the symptoms of diabetes, cancer, and or Waardenburg syndrome, wherein said pharmaceutical composition comprises an element selected from the group consisting of: a polynucleotide encoding a protein of the ONECUT family, a vector comprising said polynucleotide, the polypeptide encoded by said polynucleotide, and a cell line transformed with said vector.